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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,319	08/19/2003	Michael D. Ruff	019031-000010	3826

24239 7590 07/27/2007
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EXAMINER	
OH, SIMON J	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
07/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/643,319	RUFF ET AL.	
	Examiner	Art Unit	
	Simon J. Oh	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-46,49-53 and 55-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-46,49-53 and 55-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Papers Received

Receipt is acknowledged of the applicant's request for continued examination and petition for extension of time, both received on 02 May 2007. Receipt is acknowledged of the applicant's amendment and response, both received on 18 July 2007.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02 May 2007 has been entered.

Claim Rejections - 35 USC § 112

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejection of Claim 56 under 35 U.S.C. 112, second paragraph, as being indefinite is hereby withdrawn in view of the present amendment to that claim.

Claims 43-46, 49-53 and 56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 43 reads that the pharmaceutical substrate is free of polysaccharides, while further reciting that it may contain cellulose, which may be broadly considered to be a polysaccharide itself. As these claim limitations appear to contradict each other, the claim and all others that depend on it are considered to be indefinite.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejection of Claims 47 and 48 under 35 U.S.C. 103(a) over Norling *et al.* is rendered moot the cancellation of that claim.

The rejection of Claims 43-46, 49-53 and 55 under 35 U.S.C. 103(a) over Norling *et al.* is hereby withdrawn.

The rejection of Claims 56 and 57 under 35 U.S.C. 103(a) as being unpatentable over Norling *et al.* (U.S. Patent No. 5,958,458) in view of Ekwuribe *et al.* (U.S. Patent Application Publication No. 2003/0050228) is hereby withdrawn.

Claims 43-46, 49-53 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Busetti *et al.* (U.S. Patent No. 5,788,987) in view of Norling *et al.* (U.S. Patent No. 5,958,458)

The Busetti *et al.* patent teaches controlled release dosage forms comprising a core containing the active agent and coated with a polymeric layer (See Abstract). Suitable active

agents include peptide drugs such as insulin (See Column 4, Lines 33-38). Suitable materials for use in the core include dibasic calcium phosphate dihydrate (See Column 4, Lines 39-50). The dosage forms may be pressed into tablets or used to fill capsules (See Column 5, Lines 19-24).

The Busetti *et al.* patent does not teach the specific configuration of a dosage form having a core where the active agent is coated over a substrate.

The Norling *et al.* patent teaches a pharmaceutical multiple unit formulation in the form of coated cores. The core material is selected from various materials that include calcium carbonate, calcium silicate, calcium magnesium silicate, calcium phosphate, and kaolin (See Abstract). Various substances may be applied as coatings to the cores, including waxes, hydrogenated oils, and glyceryl monostearate. The coating material may be admixed with excipients that include colloidal silicon dioxide, talc, and magnesium stearate. The coating material may further comprise plasticizers, such as castor oil, mineral oil, and coconut oil (See Column 9, Line 41 to Column 10, Line 57). Film coatings comprising polymers such as ethylcellulose may be included in the disclosed composition (See Column 9, Lines 43-50). The disclosed composition may be embodied in various formulations, including powders, granules, tablets, as well as liquid formulations (See Column 13, Lines 29-36). The cores may also comprise an active substance, which may be coated onto the surface of the cores (See Column 11, Lines 57-67). The active substance may be selected from various broad categories of agents, including insulin (See Column 7, Lines 60-67). The patent discloses examples where inert cores are prepared and where varying amounts of various coating materials are applied to these cores (See Example 1A to Example 10). A recited feature of the disclosed invention is its control of particle size for the purpose of increasing the likelihood of patient compliance

It is the position of the examiner that the instantly claimed invention is made obvious by the disclosure of the prior art. One of ordinary skill in the art would be motivated to formulate the dosage form taught by Busetti *et al.* modified by the teachings of Norling *et al.* to create a dosage form with extended release properties with a carefully controlled particle size so as to increase the likelihood of patient compliance. As the prior art references are both drawn to dosage forms having a coated core, they are considered to be analogous. Therefore, one of ordinary skill in the art would have a reasonable expectation of success in combining the prior art references together. Furthermore, the prior art disclosure of the core material being coated with various excipients such as hydrogenated oils and magnesium stearate, it is the position of the examiner that this disclosure reads on what the applicant was chosen to define as a permeation enhancer. Thus, the instantly claimed invention is prima facie obvious.

Claims 56 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Busetti *et al.* (U.S. Patent No. 5,788,987) in view of Norling *et al.* (U.S. Patent No. 5,958,458) and Ekwuribe *et al.* (U.S. Patent Application Publication No. 2003/0050228)

The Busetti *et al.* patent teaches controlled release dosage forms comprising a core containing the active agent and coated with a polymeric layer (See Abstract). Suitable active agents include peptide drugs such as insulin (See Column 4, Lines 33-38). Suitable materials for use in the core include dibasic calcium phosphate dihydrate (See Column 4, Lines 39-50). The dosage forms may be pressed into tablets or used to fill capsules (See Column 5, Lines 19-24).

The Busetti *et al.* patent does not teach the specific configuration of a dosage form having a core where the active agent is coated over a substrate.

The Norling *et al.* patent teaches a pharmaceutical multiple unit formulation in the form of coated cores. The core material is selected from various materials that include calcium carbonate, calcium silicate, calcium magnesium silicate, calcium phosphate, and kaolin (See Abstract). Various substances may be applied as coatings to the cores, including waxes, hydrogenated oils, and glyceryl monostearate. The coating material may be admixed with excipients that include colloidal silicon dioxide, talc, and magnesium stearate. The coating material may further comprise plasticizers, such as castor oil, mineral oil, and coconut oil (See Column 9, Line 41 to Column 10, Line 57). Film coatings comprising polymers such as ethylcellulose may be included in the disclosed composition (See Column 9, Lines 43-50). The disclosed composition may be embodied in various formulations, including powders, granules, tablets, as well as liquid formulations (See Column 13, Lines 29-36). The cores may also comprise an active substance, which may be coated onto the surface of the cores (See Column 11, Lines 57-67). The active substance may be selected from various broad categories of agents, including insulin (See Column 7, Lines 60-67). The patent discloses examples where inert cores are prepared and where varying amounts of various coating materials are applied to these cores (See Example 1A to Example 10). A recited feature of the disclosed invention is its control of particle size for the purpose of increasing the likelihood of patient compliance

The Ekwuribe *et al.* reference discloses methods for the treatment of diabetes where oral compositions of insulin drugs are administered, for the purpose of administering insulin to a subject in need thereof through routes that are more convenient than the traditional method of subcutaneous administration of insulin (See Claim 1; and Sections 0003 to 0017). To this end, the Ekwuribe *et al.* reference discloses insulin polypeptides that are suitable for oral

administration, such as HIM2 (See Sections 0133 to 0134). Solid pharmaceutical formulations for oral administration such as powders and granules are disclosed (See Section 0145).

It is the position of the examiner that the instantly claimed invention is made obvious by the disclosure of the prior art. One of ordinary skill in the art would be motivated to formulate the dosage form taught by Busetti *et al.* modified by the teachings of Norling *et al.* to create a dosage form with extended release properties with a carefully controlled particle size so as to increase the likelihood of patient compliance. As the prior art references are both drawn to dosage forms having a coated core, they are considered to be analogous. Therefore, one of ordinary skill in the art would have a reasonable expectation of success in combining the prior art references together. Furthermore, the prior art disclosure of the core material being coated with various excipients such as hydrogenated oils and magnesium stearate, it is the position of the examiner that this disclosure reads on what the applicant was chosen to define as a permeation enhancer.

It is the position of the examiner that the instantly claimed invention is made obvious by the collective disclosure of the prior art. As the Busetti *et al.* patent teaches pharmaceutical compositions suitable for oral administration having a core containing an active agent such as insulin, one of ordinary skill in the art would be motivated to substitute insulin taught in the Norling *et al.* patent with the insulin polypeptides disclosed in the Ekwuribe *et al.* reference, since such insulin drugs are disclosed as being better suited for the oral administration of insulin. As both prior art references are drawn to oral pharmaceutical formulations that contain an insulin drug, they are considered analogous to one another and one of ordinary skill in the art would

therefore have a reasonable expectation of success in combining the references to arrive at the instantly claimed invention. Thus, the instantly claimed invention is prima facie obvious.

Response to Arguments

Applicant's arguments with respect to claims 42-46, 49-53 and 55-57 have been considered but are moot in view of the new ground(s) of rejection.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Simon J. Oh whose telephone number is (571) 272-0599. The examiner can normally be reached on M-F 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Simon J. Oh
Examiner
Art Unit 1618

sjo

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER